

Claims

What is claimed is:

1. A device for carrying out of investigations on living cells, cell cultures and the like, especially for the detection of metabolic activity of the cells, which are located in a liquid medium, the device includes at least a receptor for liquid medium along with the cell culture, and wherein one or more measuring apparatuses and/or sensors for measurement of the cell culture are provided and wherein a movable separation element is provided, which confiningly borders a reaction space, characterized in that, the separation element (7, 7a) is placed in a measurement position, closely above a cell culture on the bottom of the receptacle to separate a reaction space (8, 8a) from a reservoir space wherein a volume of the reservoir space is an order of magnitude greater than a volume of the reaction space (8, 8a), and the separation element (7, 7a) is movable through one of an essentially vertical up and down motion, from a bottom proximal location, which covers the cell culture and serves as the measurement position, and a bottom distal position, in at least which position, the reservoir (14, 14a) is in fluid communication with the reaction space (8, 8a), or a forward and back, lateral motion between the measurement position and a position in which the reaction space (8, 8a) is in fluid communication with the reservoir (14, 14a).

2. A device in accordance with Claim 1, characterized in that at least one separating element for one or more cell culture(s) (2) located on the bottom of the receptacle can be positioned, and in some cases in that position can be brought into such close proximity to said cell culture, as to respectively laterally displace a partial volume of the liquid culture medium (4) which covers the cell culture.

3. A device in accordance with Claim 1, characterized in that one sensor, or a multiplicity of sensors (6), is/are placed on, or in, the bottom of the receptacle (3a) and in that culture areas separated from one another, are formed especially by means of the application of structured, cell repellent coatings or created by means of a three dimensional contouring of the said bottom with recesses or elevations about the separated areas therebetween, and in that the culture medium (4) in the culture areas advantageously is respectively present as drops (25).

4. A device in accordance with Claim 1, characterized in that the bottom of the receptacle is formed by at least one part of at least one of the wafers which possess the sensor(s) (6).

5. A device in accordance with Claim 1, characterized in that an open top container, is provided as a receptacle (3), into which a separating element (7) extends, which divides the space of the entire receptacle (3) into two space portions, one positioned above the other, and in that the bottom side space portion forms a small volume reaction space (8) in comparison to the entire volume of the receptacle (3) and the other space portion forms a reservoir (14) and in that at least one flow channel (9) is provided, which first, communicates with the reaction space (8) and second, communicates with the reservoir space (14) and in that within the separating element (7) one or more through-flow channels (15) are provided, which open into the small volume reaction space (8) of the receptacle (3) and/or in the reservoir space (14) of the receptacle (3).

6. A device in accordance with Claim 1, characterized in that one or more sensors (6) and/or measurement apparatuses are placed in the area of the reaction space (8, 8a).

7. A device in accordance with Claim 5, characterized in that the separating element (7) within the receptacle (3) is movable, back and forth, between a position proximal to the bottom and a position remote from the bottom and in the position proximal to the bottom borders the reaction space (8).

8. A device in accordance with Claim 1, characterized in that the side of the separating element (7) proximal to the bottom, possesses a cover, that is, a bordering surface, for the measurement of the substances consumed or produced by the cells, especially a surface corresponding to the sensor surface.

9. A device in accordance with Claim 5, characterized in that the separating element (7) can be inserted from above into the receptacle (3).

10. A device in accordance with Claim 1, characterized in that the distance of the separating element (7) from the cell culture (2) and therewith the bottom proximal position of the said separating element (7) is adjustable.

11. A device in accordance with Claim 5, characterized in that the separating element (7) is advantageously constructed in the shape of a hand stamp and has a head (10) with approximately the same cross-section as that of the receptacle (3), and which separating element (7) divides the said receptacle into a reaction space (8) and a reservoir (14) and in that on the separating element (7) a shaft (11) is connected which extends to the outside, the outside cross-section of which shaft (11) is smaller than the open inside cross-section of the receptacle (3) and in that the intervening space between the shaft and the inner wall of the receptacle (3) forms the reservoir (14).

12. A device in accordance with Claim 5, characterized in that within the separating element (7) one or more flow channels are provided which first, open in the reaction space (8) and second open in the reservoir space (14).

13. A device in accordance with Claim 5, characterized in that the flow channel (9) is formed by an annular gap provided between the separating element (7) and the inner wall of the receptacle (3) or is designed as a rim profiling, and in that this flow channel, or flow channels remain(s) available, in the case of a separating element (7) which can be adjusted as to height, at least within the lift interval between a position proximal to the bottom and a position remote therefrom.

14. A device in accordance with Claim 1, characterized in that the underside of the separating element (7) possesses a contouring for the guidance of gas bubbles to the outside, this being preferably a convex bulging.

15. A device in accordance with Claim 5, characterized in that a thrust limitation for the separating element (7) is provided and in that for this purpose, in the bottom proximal position an effective restraint is placed on the separating element (7), preferably this being a detent abutted by the upper rim (12) of the receptacle (3).

16. A device in accordance with Claim 16, characterized in that the detent placed on the upper receptacle rim (12) by the separating element (7) is made by means of a cover (13) which overlaps the rim (12) of the receptacle (3) or alternately by a cover (13) with a conical section which engages in a counter conical section of the receptacle opening.

17. A device in accordance with Claim 1, characterized in that the separating element (7) possesses on its upper side, an especially standard opening, preferably of a receiving conical shape for the coupling with a pipette, a pipette tip, or a dispenser channel.

18. A device in accordance with Claim 5, characterized in that the receiving

volume of the reservoir (14, 14a) is multiply greater than the receiving volume of the reaction space (8, 8a) and that these two volumes are in relation to one another by the ratios of respectively, 10 : 1 to approximately 100 : 1.

19. A device in accordance with Claim 1, characterized in that at least on the bottom of the receptacle (3) or a receiver, is placed at least one chip with one or preferably several microsensors.

20. A device in accordance with Claim 1, characterized in that on the separating element (7), proximal to the reaction space (8) and/or to the reservoir (14), sensors (6) and/or electrodes are provided.

21. A device in accordance with Claim 5, characterized in that at a distance from the receptacle bottom and between this and the separating element (7) in its bottom proximal position, a microporous membrane (23) or a similar filter or protective covering for the cell culture is provided.

22. A device in accordance with Claim 1, characterized in that the separating element (7) is comprised of a smooth, cell rejecting, inert and easily sterilized material, this being preferably polytetrafluor ethylene.

23. A device in accordance with Claim 1, characterized in that the resting surface for the cell culture (2) is optically transparent and in that the resting surface is related to an optical measuring apparatus, which, preferably, is situated on the underside.

24. A device in accordance with Claim 1, characterized in that a plurality of receptacles (3) are provided, preferably as a part of a pipetting automat (19) and in that these receptacles (3) are especially made by commercially available multiwell plates (20) and in that on the lower ends of the dispenser channels of the pipetting automat,

respectively, the separating element (7) is provided.

25. A device in accordance with Claim 1, characterized in that the separating element (7) on its end distal to the bottom, possesses a fitting for connecting to, or plugging into, a dispenser channel (22), preferably a pipetting automat.